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Methanol poisoning during COVID-19 pandemic; A systematic scoping review

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ABSTRACT

Objective: In this systematic scoping review, it was aimed to assess the epidemiology of methanol poisoning, clinical findings and patients' management, causes, and recommendations regarding prevention or reduction of methanol poisoning during COVID-19 pandemic.

Methods: Three Electronic databases [Medline (accessed from PubMed), Scopus, and Science Direct] were searched systematically from December 01, 2019 to September 10, 2020, using MESH terms and the related keywords in English language. Considering the titles and abstracts, unrelated studies were excluded. The full texts of the remained studies were evaluated by authors, independently. Then, the studies' findings were assessed and reported.

Results: Total of 86 articles were obtained within the first step of searching, and 64 ones remained after removing the duplications. Through the title and abstract screening, 35 were removed. Finally, after reading the full text of the remained articles, 15 ones included in data extraction. Most of the previous reported evidence (13/15) were letter to editor, commentary and short reports. None of them were interventional, and none of them followed the patients. Findings were summarized in four categories: 1) epidemiology; 2) clinical findings and patients' management; 3) causes; and 4) recommendation regarding prevention or reduction of methanol poisoning during COVID-19 pandemic.

Conclusion: The recent outbreak is the largest methanol mass poisoning outbreak throughout Iran and the world in recent decades. The causes of methanol poisoning during the COVID-19 pandemic are intertwined, and most of them are modifiable by health policy makers. Building trust, educating and warning, as well as controlling and monitoring are three main recommendation for prevention or reduction of methanol poisoning.

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1. Introduction

The coronavirus disease 2019 (COVID-19) is an infectious disease that first appeared in December 2019 in China. Symptoms of the virus range from mild to severe disease, and in some cases can be fatal [1,2]. The long-term effects of COVID-19 on physical and mental health are

still under study [3]. This new health issue has clinical, psychological, and emotional consequences, the collapse of the health system, and economic slowdown for the international communities [4,5]. The World Health Organization (WHO) has proposed preventive measures and a healthy lifestyle with an effective immune system to fight and protect against this infection. One of the best recommendations of this organization is to disinfect hands with soap or 60% alcohol disinfectant [6]. Also, Center for Disease Control and Prevention (CDC) has recommended the use of hand sanitizers with a greater than 60% ethanol or 70% isopropanol for hand hygiene [7].

Although wide ranges of disinfection detergents are available, alcoholic disinfectants are the best for viruses [8]. But, some hand sanitizer

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products may contain unacceptable active ingredients (especially methanol) other than the recommended alcohols (ethanol or isopropyl alcohol), which can be toxic due to respiratory and dermal exposure, and it may lead death if swallowed [9]. Alcohol (ethanol) is a substance in alcoholic beverages, too. Other toxins that may have an ethanol odor may be added to fake beverages produced informally or illegally, or may be present in alcoholic beverages not intended for human consumption, such as hand sanitizers [10]. One of these similar substances is methanol (also known as methyl alcohol or wood alcohol), which is commonly available chemical with a variety of uses as a solvent, in chemical synthesis, and as a fuel [11,12].

Although products containing methanol are easily available, but illicit and informal productions are responsible for most methanol poisoning [13]. Methanol is highly toxic with high mortality and morbidity (including vision problems, especially blindness, metabolic, cardiac, and extensive neurological disorders) even after hospital discharge [14–17]. Hemorrhagic and non-hemorrhagic necrotic of basal ganglia, white matter necrosis and diffuse cerebral edema may lead to a serious prognosis [18,19]. Methanol poisoning is mostly occurred by direct consumption in doses as small as 15 mL and rarely through inhalation or skin absorption that it has little toxicity. But when it was metabolized into products, it is highly toxic especially for central nerve and gastrointestinal systems [10,12,14,15]. This substance is rapidly absorbed from the gastrointestinal tract in less than 10 min and reaches the peak plasma concentration in 30 min to one hour [13].

With the onset of the COVID-19 pandemic, misinformation about the alcohol's potential to neutralize this virus, led to a significant increase in methanol-induced mortality. Reports as of April 27, 2020 from the Ministry of Health of Iran showed 5011 patients with methanol poisoning, with 505 confirmed deaths. The total number of deaths from February to April 2020 was almost eight times higher than the corresponding number of confirmed deaths for the same period in 2019, but reports before 2019 show fewer mortality due to methanol poisoning [20]. The recent and perhaps most important outbreak coincided with the COVID-19 pandemic [21]. In some provinces in Iran, for example in Fars province, southern Iran, the total mortality rate from methanol poisoning was higher than COVID-19, which many reasons were presented in various studies. One reason was that the death from alcohol poisoning happens more quickly than death from COVID-19 [22]. Also, outbreaks of methanol poisoning in Iran in 2007, 2013 and 2018, led to significant complications and mortality [19,21,23]. In Norway (2002–2004), 59 poisoned patients were reported with 17 deaths [14]. Likewise, outbreaks were reported in the Czech Republic, Estonia, Libya, Kenya, Malaysia, and other countries with fewer death [24–27].

In this systematic scoping review, it was aimed to assess the epidemiology of methanol poisoning, clinical findings and patients' management, causes, as well as recommendations regarding prevention or reduction of methanol poisoning during COVID-19 pandemic.

2. Methods

The present systematic scoping review was conducted based on the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) statement [28].

2.1. Data sources

As was shown in Fig. 1, a multi-step search strategy was performed. The electronic literature searches were conducted to identify all relevant studies on MEDLINE (accessed from PubMed), Science Direct, and Scopus electronic databases from December 01, 2019 to September 10, 2020, using MESH terms and the related keywords (Table 1). Google Scholar and researchgate.net were also reviewed manually to explore the grey literature in English. To ensure literature saturation, the reference lists of the included studies or relevant reviews identified through

the search were scanned. All the following searches were conducted by three authors [MA, RSM, HS].

2.2. Study eligibility criteria

We focused on the studies on the epidemiology, clinical findings and patients' management, causes, as well as recommendations regarding prevention or reduction of methanol poisoning during COVID-19 pandemic. Articles were excluded if they were not relevant, or were performed before the COVID-19 pandemic, through reading the titles and the abstracts [RSM, MA, RSM].

2.3. Participants, and interventions

The target population were all patients around the world with methanol poisoning.

2.4. Study appraisal and synthesis methods

Full texts of the studies were evaluated by three authors [RSM, MA, RSM]; they decided whether these met the inclusion criteria, independently. They resolved any disagreement through discussions, and finally the articles were selected based on consensus. Neither of the authors were blind to the journal titles or to the study authors or institutions. Then, the level of evidence of each study was determined [29]. The following data were extracted from the included studies and recorded in a Microsoft Excel sheet, 2016: study authors, country, title, and main findings [RSM, MA, HS].

2.5. Ethical issues

Ethical issues (including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

3. Results

In total, 86 (23 articles in Medline, 24 articles in Scopus, 16 article from Science Direct, and 23 articles from other resources) were achieved at the first step search. After initial assessment 22 duplications were found. After the identification and the screening, 29 articles were selected as potential studies. After reading the full text of these articles, 15 articles formed the final sample and considered for the final data extraction [5,10,19,21,22,30–39]. Inter-rater agreement following the first round of screening between the investigators was 95.31% (Cohen's $k = 0.89$). Within the second round of screening, inter-rater agreement rose to 100%. Table 2 shows the summary of these studies.

Fourteen (14/15) studies were peer-reviewed [5,10,19,21,22,30–38] and 1/15 of them was in-review [39]. Our investigation illustrated that the most of available reported evidences (13/15) were in the format of letter to editor, commentary and short reports [5,10,19,21,22,30–34,36–38], and only 2/15 were original articles [35,40]. None of the studies were interventional, and none of them followed the patients. As was shown in Table 3, most of the studies (12/15) were reported from Iran [5,10,19,21,22,30,32–39].

We summarized the results in four categories: 1) epidemiology; 2) clinical findings and patients' management; 3) causes; and 4) recommendation regarding prevention or reduction of methanol poisoning during COVID-19 pandemic. All studies mentioned the clinical and paraclinical findings in these patients, which were shown in Table 4. Visual impairment, severe anion-gap metabolic acidosis, gastrointestinal symptoms, and death were the most suggestive findings in patients with methanol poisoning. Suggestive treatments in patients with methanol poisoning is shown in Table 5. The causes of methanol poisoning during COVID-19 pandemic were disused in 12/15 studies [5,10,19,21,22,30,32–34,36–38], which we categorized them in

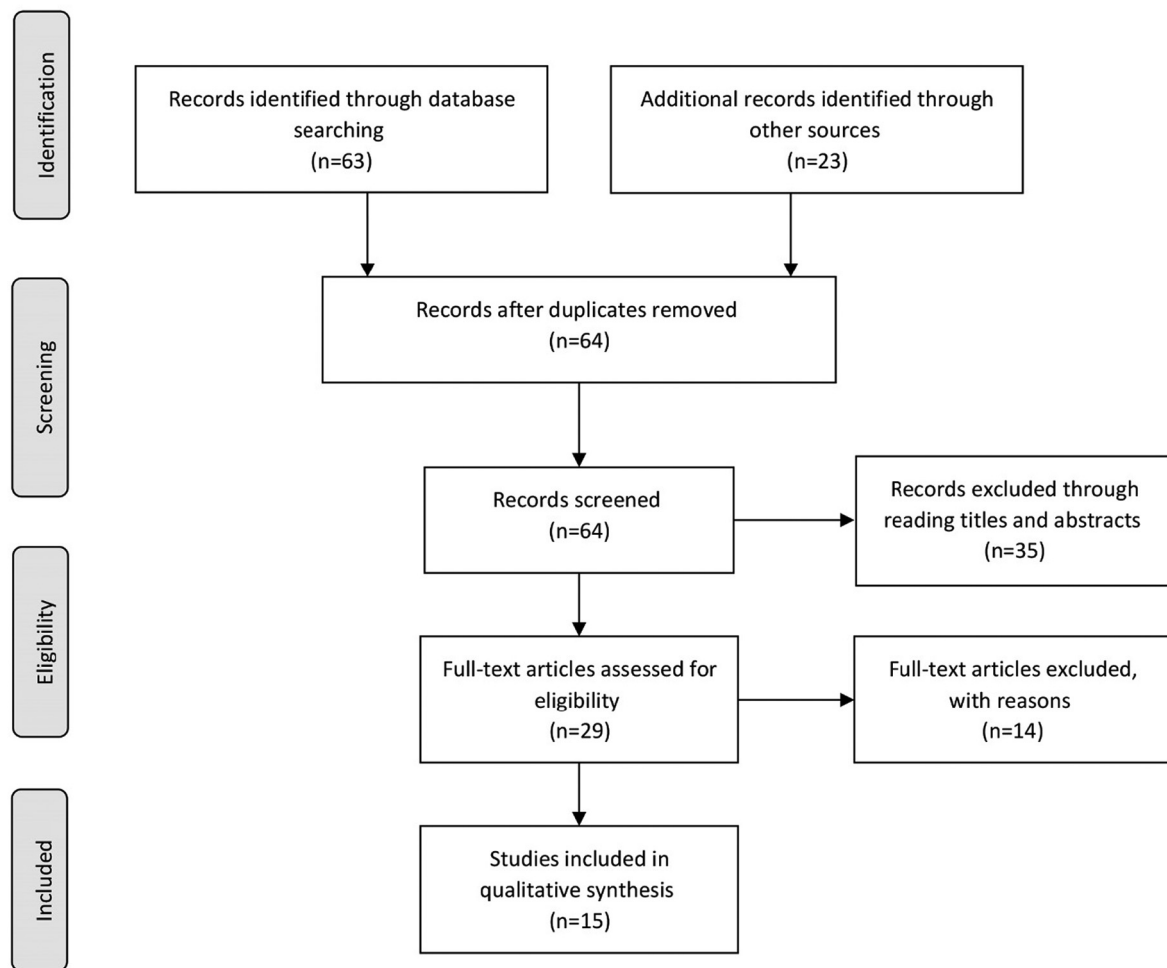


Fig. 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram of the study.

three areas (3P): a) public; b) physicians; and c) policy makers (Table 6). Moreover, 13/15 studies had recommendations for prevention or reduction of methanol poisoning during COVID-19 pandemic [5,10,19,21,22,30–34,36–38], which we categorized them in three areas (3P): a) public; b) physicians; and c) policy makers (Table 7). Fig. 2 shows the mapping of recommendations for policy makers in three categories; a) building trust; b) educating and warning; and c) controlling and monitoring.

Table 1
Search strategy used in the present study.

PubMed:
((covid-19[Title] OR corona virus[Title] OR SARS-CoV-2[Title] OR pandemic*[Title] OR outbreak[Title]) AND (toxic*[Title/Abstract] OR poison*[Title/Abstract] OR adverse effect[Title/Abstract] OR death*[Title/Abstract] OR Swallowing[Text Word] OR blindness[Text Word] OR conscious*[Text Word] OR coordination[Text Word] OR vomit*[Text Word] OR abdominal pain[Text Word] OR vision*[Text Word] OR impairment*[Text Word])) AND (Methanol[Title/Abstract] OR Methanol[MeSH Terms] or Carbinol[Title/Abstract] OR Wood Alcohol[Title/Abstract] OR Methyl Alcohol[Title/Abstract] OR Sodium Methoxide[Title/Abstract] OR disinfectant [Title/Abstract] OR methyl alcohol[Title/Abstract] OR disinfectant[Title/Abstract] OR sanitizer[Title/Abstract] OR cleansing[Title/Abstract])
Scopus:
TITLE(covid OR corona OR sars cov 2) AND TITLE-ABS-KEY(methanol OR alcohol)
Science Direct: Title, abstract, keywords: methanol, Title: covid OR corona OR sars-cov-2"
Scopus: TITLE(covid OR corona OR sars cov 2) AND TITLE-ABS-KEY(methanol OR alcohol)

4. Discussion

In this systematic scoping review, fifteen studies were assessed, which that the obtained results were summarized in four areas. Here we will discuss the findings.

4.1. Epidemiology

It was reported from Iranian Legal Medicine Organization that all provinces in Iran experienced methanol poisoning, which from March to April 2020 increase 11 fold in comparison to the same period of last year [22]. Moreover, it was reported that formal statistics about methanol intoxication and mortality are not easily available and it might be under estimated. But, all regions in Iran were involved. Khuzestan, Fars, and Tehran were the most affected regions [19,32]. It was informed that 5876 patients were hospitalized until May 2, 2020, 534 were confirmed dead in the hospital reported by Iran Ministry of Health, and 800 deaths confirmed by Iranian legal Medical Organization, which includes out-of-hospital deaths [19]. An estimated mortality rate in Iran was in the range of 9–14% [19,21,37]. Tehran province was reported the highest number of deaths (absolute number of 192 cases). In Fars province, the fatality rate from methanol poisoning reached 12.6%, but only 2.7% died from COVID-19 [22]. Arasteh et al. stated that more than 200 patients were admitted as methanol poisoning in one week in the emergency departments of Namazi Hospital, affiliated to Shiraz University of Medical Sciences in Southern Iran [5]. It was reported that the age of poisoned patients in Iran ranged between 14 and

Table 2

An overview of studies included in this systematic scoping review and their main findings

Author	Country	Title	Epidemiology	Clinical findings	Patients' management	Causes	Recommendations	Level of evidence
Aghababaeian et al. [22] (2020)	Iran	Alcohol intake in an attempt to fight COVID-19: A medical myth in Iran.	<ul style="list-style-type: none"> • More than 3000 people poisoned by methanol in all Iranian provinces (March–April 2020). • 1066 were hospitalized, 73 were admitted to intensive care units, and 728 had died. • The age of the methanol poisoning was ranged 14–78 years. • Tehran province recorded the highest number of deaths (192 cases). • The fatality rate from methanol poisoning reached 12.6% in Fars province. 	NR	NR	<ul style="list-style-type: none"> • Lack of public awareness about the prevention and treatment of COVID-19. • Lack of public awareness about the different types and uses of alcohol. • Large industrial using ethanol for the manufacturing of hand sanitizers during the COVID-19 pandemic, following the shortage of it, shift people to use methanol instead of ethanol for the manufacturing of alcohol beverages. • Banning of selling, consuming, producing, and distributing alcoholic beverages in some counties. • Access smuggled or illegally homemade alcoholic beverages that may use methanol instead of ethanol. • Adding bleach to methanol to make it colorless by alcohol bootleggers and selling it as ethanol. • Not trust the organizations or agencies publishing the true information. • Tend to rumors, myths and conflicting information, and harmful practices from unofficial communication channels and social media that encouraged people to drink or gargle alcohol to prevent or cure COVID-19. • Fear of being arrested when going to hospitals. 	<ul style="list-style-type: none"> • Adding color to methanol by manufacturers, so people can easily differentiate between methanol and ethanol (colorless). • Alert people by internationally recognized references and guidelines to not to use methanol for disinfecting hands, skin, medical supplies, and surfaces (such as door handles, desks, floors, etc.). • Buying only standardized products containing alcohol (ethanol) for disinfection from reliable sources. • Monitoring rumors via mainstream media, hotlines, social media, SMS messages, focus groups, feedback from community influencers and community volunteers. • Educating people about different types of alcohol and the related health impacts, even if consuming alcohol is prohibited. • Informing people that the available “ethanol” might actually be methanol. • Informed people that there is no policy in the hospitals in Iran to report alcohol users to the justice authorities and that this information is considered highly confidential. • Publishing updates of affected population by emergency management officials about risk management and health and safety issues to mitigate uncertainty and rumors. • Encouraging the public by emergency management officials to remain skeptical about information coming from unofficial channels. • Including social media strategy in effective communication plan. • Improvement the surveillance and early warning systems for alcohol poisoning. • Cooperation between authorities at the local, national, and international levels to combat the illicit alcohol. 	VII

Arasteh et al. [5] (2020)	Iran	A surge in methanol poisoning amid COVID-19 pandemic: why is this occurring?	<ul style="list-style-type: none"> • More than 200 patients (unpublished data) were admitted in one week time in the emergency departments of Namazi Hospital, affiliated by Shiraz University of Medical sciences in Southern Iran. 	NR	NR	<ul style="list-style-type: none"> • Obtaining alcoholic drinks in Iran is far more difficult than in other countries in which the sale of alcoholic beverages is legal. • Shifting the use of methanol instead of ethanol by individuals who were previously using ethanol for the manufacturing of alcohol beverages due to unprecedented shortage in ethanol because of the large industrial use of ethanol for the manufacturing of hand sanitizers. • Public misconception about drinking alcohol-based that may be protective against COVID-19. • Decreasing sports activity due to closure of gyms and the mass advertisement to the public to remain home have all led to increased use of alcohol drinks. 	<ul style="list-style-type: none"> • Increasing unstructured leisure time. 	VII
Banagozar Mohammadi, A and Vahabzadeh M [30] (2020)	Iran	A concurrent outbreak of COVID-19 and methanol poisoning in Iran: is this the time to make amendments to alcohol drinking laws?	<ul style="list-style-type: none"> • No accurate number for methanol poisonings throughout the COVID-19 pandemic due to lack of a comprehensive toxicology registry system in Iran. • Methanol poisoning might be under estimated. • Morbidity and mortality in methanol poisoning are most prevalent amongst young and healthy people. 	<ul style="list-style-type: none"> • End organ failure • Blindness • GI symptoms like nausea and vomiting • Death 	<ul style="list-style-type: none"> • Direct relationship between the degree of side effects and availability of treatment. 	<ul style="list-style-type: none"> • Misleading and false information in social media regarding the disinfecting effect of alcohol ingestion on viruses entering the GI tract. • Drinking alcohol in the hope of disinfecting the virus within their bodies. • Law prohibition of any production, consumption or distribution of alcoholic beverages is prohibited since 1979 in Iran. • Alcoholic beverage through unlawful means such as personal home production and illegal imports from some neighboring countries. • Providing sub-standard alcohols as a toxic mixture of methanol and ethanol to illegal consumers due to a vicious cycle of supply and demand. • Controlling the quality of alcoholic beverages by Food and Drug Administration • Increasing the risk of toxic alcohol poisoning due to situations like COVID-related lockdown and stress. 	<ul style="list-style-type: none"> • Developing appropriate scientific policies for the prevention of alcohol poisoning. • Making proper arrangement and policies for alcohol consumption and trade. • Providing appropriate information for citizens. • Providing essential facilities for timely diagnosis and treatment of poisonings. • Providing proper training of poisoning course in medical education. • Making amendments to the law for production, sale, and consumption of alcohols in order to improve the society health and prevent the production of toxic alcohols as beverages by legislators in Iran. • Making strengthen supervision over pharmaceutical companies for production of alcohol containing products by the Food and Drug Administration of Iran. 	VII

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Table 2 (continued)

Author	Country	Title	Epidemiology	Clinical findings	Patients' management	Causes	Recommendations	Level of evidence
Dear et al. [31] (2020)	Australia	Potential methanol toxicity and the importance of using a standardized alcohol-based hand rub formulation in the era of COVID-19.	<ul style="list-style-type: none"> One patient with methanol poisoning due to ingestion of the contents of methylated with containing of more than 60% methanol. 	<ul style="list-style-type: none"> Nausea Vomiting Abdominal pain Central nervous system depression Visual disturbance Increased osmolar gap with metabolic acidosis 	NR	NR	<ul style="list-style-type: none"> Not use methylated spirits in alcohol-based hand rubs. Avoiding general public from producing their own alcohol-based hand rubs. Adhering to the WHO guidance on formulations of alcohol-based hand rubs. 	VII
Delirrad M and Banagozar Mohammadi A [32] (2020)	Iran	New methanol poisoning outbreaks in Iran following COVID-19 pandemic.	<ul style="list-style-type: none"> Not easily accessible formal statistics about methanol poisoning and its mortality. All regions of the Iran were involved. The most affected provinces were Khuzestan, Fars, Tehran, East Azerbaijan, Alborz, Khorasan and Ardebil. Total number of patients attending hospital due to toxic alcohols reached more than 2500 patients in one month. About 500 patients have died. 	<ul style="list-style-type: none"> Blindness Death 	<ul style="list-style-type: none"> Not having proper laboratory equipment to determine the blood concentration of toxic alcohols. Requiring antidotes and medications for the treatment of the patients. 	<ul style="list-style-type: none"> Different consequences of the disease in Iran from other countries, because of US sanctions on access to essential medicines and equipment, faulty understanding and mismanagement by the ruling authorities Public unawareness and mistaken beliefs regarding alcohol as a protective agent. Society unawareness about the hazards of toxic alcohol with the spread of fake news and recommendations across social media. Fake news about the efficacy of various substances for the treatment or prevention of COVID-19 across social media. Recommendations on the use of alcohol for controlling the disease. Gurgling or drinking alcoholic beverages for disinfection of the mouth or inside the body and prevent the infection by killing the viruses. Legal prohibiting of the production, distribution, and drinking of alcoholic beverages are in Iran. Making consumed alcoholic drinks at home or unauthorized workrooms and repackaged in famous brands containers. Smuggled and illegally distribution of alcohol. 	<ul style="list-style-type: none"> Prosecuting ruling authorities for the methanol outbreaks. 	
Hassanian-Moghaddam et al. [19] (2020)	Iran	Double trouble: methanol outbreak in the wake of the COVID-19 pandemic in Iran-a cross-sectional assessment.	<ul style="list-style-type: none"> 5876 hospitalizations due to methanol poisoning until May 2, 2020. Majority of them (3068 = in three (Tehran, Fars, Khuzestan) out of the total 31 Iranian provinces. 	<ul style="list-style-type: none"> Visual impairment Blindness 	<ul style="list-style-type: none"> Difficult and complicated hospital-based diagnosis of methanol poisoning due to lack of diagnostic equipment or physician knowledge. 	<ul style="list-style-type: none"> Using adulterated alcohol for recreational purposes or as gastrointestinal disinfectant to prevent or treat COVID-19 infection. 	<ul style="list-style-type: none"> Importance of early identification and initiation of treatment, which can be supplemented by “active case finding” by treating physicians and public health agencies. Messaging public health and improvement of strategic 	VI

Iranpour et al. [33] (2020)	Iran	Methanol poisoning emerging as the result of COVID-19 outbreak; radiologic perspective.	<ul style="list-style-type: none"> • 534 were confirmed dead in the hospital reported by Iran Ministry of Health (Case fatality rate of approximately 9%). • 800 deaths confirmed by Iranian legal Medical Organization, which includes out-of-hospital deaths (Case fatality rate of approximately 14%). • An estimated mortality rate in the range of 9–14%. 	NR	<ul style="list-style-type: none"> • Neurological signs and symptoms • Different degrees of decrease in the level of consciousness • Headache • Vertigo • Impaired vision • An axial nonenhanced brain computed tomography scan: • Bilateral symmetrical decreased density of lentiform nuclei, especially putamina • Massive hemorrhage in the left lentiform nucleus • Axial T2 weighted MR images of the brain: • Increased signal intensity on T2-weighted sequence • Diffusion weighted imaging • Symmetrical increased signal intensity of basal ganglia • Putaminal involvement • Resorption of infarcted putamen in later stages • Death 	<ul style="list-style-type: none"> • Administration of an alcohol dehydrogenase inhibitor, such as fomepizole or ethanol. • Controversy about the value of hemodialysis (restricting it to specific cases especially in severe intoxication). 	<ul style="list-style-type: none"> • False rumor has circulated that drinking alcohol is beneficial in preventing or curing a possible infection. 	<ul style="list-style-type: none"> • Familiarity of the clinicians especially those working in emergency departments with clinical and radiological presentations of methanol poisoning, which delayed diagnosis and treatment result in high mortality. • Public health education. • Appropriate preventive measures based on scientific principles to prevent further morbidity and mortality. 	VII
Mehrpour O and Sadeghi M [34] (2020)	Iran	Toll of acute methanol poisoning for preventing COVID-19.	700 death up to April 20, 2020 due to ingestion of denatured alcohol in an attempt to fight COVID-19.	NR	<ul style="list-style-type: none"> • Death 	NR	<ul style="list-style-type: none"> • Unfounded rumors circulated on social media that drinking or gargling alcohol could prevent or cure COVID-19. • False assumption that drinking alcohol would kill the virus. • Reduction in the amount of ethanol on the market. • Using bleach to mask the color of industrial methanol solutions in order to sell the colorless methyl alcohol instead of drinkable ethanol by individual opportunistic. 	<ul style="list-style-type: none"> • Exerting every effort to dispel dangerous and unscientific misinformation. • Exposing misinformation and false rumors in order to protect people and prevent more damage to their health and to the ability of hospitals to function effectively. • Following recommended medical advice to protect themselves and their families from becoming infected by people. 	VII
Nikoo et al. [35] (2020)	Iran	Electrocardiographic findings of methanol toxicity: a cross-sectional study of 356 cases in Iran	<ul style="list-style-type: none"> • Hospitalization of 356 patients with methanol poisoning in Faghihi and Namazi Hospitals, affiliated by Shiraz University 	<ul style="list-style-type: none"> • The most common ECG findings: • J point elevation (68.8%) • U wave (59.2%) • QTc prolongation (53.2% in 	<ul style="list-style-type: none"> • Four independent factors correlated with methanol toxicity severity: Severe acidosis (pH < 7) with 	NR	NR	NR	VI

(continued on next page)

Table 2 (continued)

Author	Country	Title	Epidemiology	Clinical findings	Patients' management	Causes	Recommendations	Level of evidence
Nikoo et al. [39] (2020)	Iran	Brugada Phenocopy in methanol toxicity: A novel marker of mortality.	<ul style="list-style-type: none"> Hospitalization of 356 patients with diagnosis of methanol poisoning in Shiraz Faghihi and Namazi Hospitals, southern Iran, during March and April 2020. 	<p>of Medical Science in March and April 2020.</p> <ul style="list-style-type: none"> men and 28.6% in women) Fragmented QRS (33.7%) Brugada pattern (8.1%) Myocardial infarction (5.3%) Osborn wave (3.7%) Severe acidosis (PH < 7) with QTc > 500 (OR = 3.15), atrioventricular block (OR = 4.46), sinus tachycardia (OR = 2.32), and ST elevation myocardial infarction (OR = 12.82) were four independent factors correlated with methanol toxicity severity. 	<ul style="list-style-type: none"> QTc > 500, atrioventricular block, sinus tachycardia, and ST elevation myocardial infarction. 	NR	NR	VI
Sefidbakht et al. [21] (2020)	Iran	Methanol toxicity outbreak: when fear of COVID-19 goes viral.	<ul style="list-style-type: none"> 797 patients with methanol poisoning with 97 deaths in Fars province, Iran in March and April 2020. 	<ul style="list-style-type: none"> Triad of visual impairment, gastrointestinal symptoms and metabolic acidosis in 6–24 h. Gastrointestinal tract involvement Central nervous system involvement: Hemorrhagic and non--hemorrhagic necrosis of basal ganglia White matter necrosis Diffuse brain edema 	NR	<ul style="list-style-type: none"> Belief that consumption of disinfectants and sanitizers, specifically, alcohol, would be beneficial in preventing the COVID-19. Several cases of methanol poisoning in children resulting from a desperate attempt by parents to prevent or cure the infection. 	<ul style="list-style-type: none"> Appropriate public education to fight the misinformation that is being spread through social media about the alcohol and other similar disinfecting agents. 	VII
Shokoohi et al. [36] (2020)	Iran	A syndemic of COVID-19 and methanol poisoning in Iran: Time for Iran to consider alcohol use as a public health challenge?	<ul style="list-style-type: none"> 3100 patients with methanol poisoning from February 19, 2020 to April 7, 2020 according to Iran's Ministry of Health. 5011 cases, with 525 confirmed deaths until April 27, 2020 according to Iran's Ministry of Health. 728 deaths (627 men and 101 women) out of the total number of patients with methanol poisoning. 471 confirmed cases (422 men and 49 women) according to Iran's Legal Medicine 	NR	Palliative care	<ul style="list-style-type: none"> Association of COVID-19 outbreak with significant public fear in Iran. The shortage of medical care and diagnostic capacity to prevent COVID-19. International economic sanctions in Iran. Limited public knowledge resulted in misinformation. Alcohol becoming more available to people and more accessible for them to buy from drugstores, as justified for sanitization for COVID-19. Gargling or drinking alcohol to disinfect and prevent COVID-19 Banning the use of alcohol use in Iran, so people are more 	<ul style="list-style-type: none"> Development and support of alcohol use-related public health models to better support public education and increase awareness. Development of national guidelines in managing mass methanol-poisoning outbreaks. Development and implementation of public health programs to better respond to ongoing alcohol use disorders, as well as better responding during times of crisis. 	VII

			<ul style="list-style-type: none"> Organization (LMO). Eight provinces being more severely affected by methanol poisoning. 			<ul style="list-style-type: none"> likely to consume bootleg alcohols that may include higher levels of methanol. Increased accessibility and consumption of mainly methanol-containing home-made and bootleg types of alcohol. 		
Soltaninejad [37] (2020)	Iran	Methanol mass poisoning outbreak, a consequence of COVID-19 pandemic and misleading messages on social media.	<ul style="list-style-type: none"> 2200 patients with methanol poisoning due to oral ingestion of illicit alcoholic beverages as of March 28, 2020. 824 (37.5%) of them were admitted to Intensive Care Unit (ICU). 296 died (fatality rate of 13.5%). More than 90% of were men mostly aged 20–30 (range 5–72) years. The poisoning has reported from 18/31 (58%) provinces of Iran. 2197 poisoned cases and 296 fatalities during 1-month period. The average mortality rate: 12.1% (approximately twice the rate of COVID-19 in Iran). 	NR	NR	<ul style="list-style-type: none"> Drinking alcohol du to suggestion in social media messages, to prevent them being infected by COVID-19 High concentrations of methanol in the counterfeit alcoholic beverages. Using methanol instead of ethanol because of its lower price and availability. Discolor the industrial alcohol by 5% sodium hypochlorite solution (Vitex®) and sale it instead of ethanol or drinking alcohol by profiteers. 	<ul style="list-style-type: none"> Raising public awareness about the fatal outcomes of consumption of counterfeit alcoholic beverages sold in the black market through broadcasting various educational programs. 	VII
Welle L. and Medoro A. [10] (2021)	USA	Tainted hand sanitizer leads to outbreak of methanol toxicity during SARS-CoV-2 pandemic.	<ul style="list-style-type: none"> 9 patients with methanol poisoning in New Mexico. 	<ul style="list-style-type: none"> Blindness (2 patients) Death (7 patients) Anion gap metabolic acidosis 	<ul style="list-style-type: none"> Fomepizole Poison Center consultation Ethanol 	<ul style="list-style-type: none"> Limit access to alcohol in the prohibition-era and in resource-poor populations turning to alternative alcohol sources. Selling and using hand sanitizers contain up to 81% methanol. 	<ul style="list-style-type: none"> Having heightened awareness by emergency physicians for methanol toxicity in at-risk populations. 	VII
Yip et al. [38] (2020)	USA	Serious Adverse Health Events, Including Death, Associated with Ingesting Alcohol-Based Hand Sanitizers Containing Methanol - Arizona and New Mexico, May–June 2020	<ul style="list-style-type: none"> 15 adult patients with methanol poisoning due to ingestion of alcohol--based hand sanitizer by reviewed 62 poison center call records from May 1 to June 30, 2020. 	<ul style="list-style-type: none"> Unresponsive seizures Unconsciousness Altered mental status Headache Decreased responsiveness Permanent disability Visual disturbance Blindness Near-total vision loss Gastrointestinal problems like abdominal pain, nausea and vomiting Dyspnea Severe anion-gap metabolic acidosis Death 	Treatment includes: <ul style="list-style-type: none"> Supportive care Correction of acidosis Administration of an alcohol dehydrogenase inhibitor (e.g., fomepizole: a competitive inhibitor of alcohol dehydrogenase Frequently hemodialysis 	<ul style="list-style-type: none"> Ingestion of alcohol-based hand sanitizers. Challenge in the clinical diagnosis of methanol poisoning due to: Challenge in the taking an exposure history in patients with altered mental status. Unable to test for a blood methanol level in some hospitals. Fear from recognition or reporting to poison centers or state health departments in poisoned patients. 	<ul style="list-style-type: none"> Warning about specific hand sanitizers that contain methanol. Never ingestion of alcohol--based hand sanitizer. Avoiding use of specific imported products found to contain methanol. Continuing to monitor Food and Drugs Administration's guidance. Having high index of suspicion for methanol poisoning by physicians when evaluating adult or pediatric patients with reported swallowing of an alcohol-based hand sanitizer product or with symptoms, signs, and laboratory findings compatible with 	VII

(continued on next page)

Table 2 (continued)

Author	Country	Title	Epidemiology	Clinical findings	Patients' management	Causes	Recommendations	Level of evidence
							<p>methanol poisoning.</p> <ul style="list-style-type: none"> • Obtaining medical management advice by physicians from their regional poison center. • Using all alcohol-based hand sanitizers only for disinfecting hands and should never be swallowed. • Stop using alcohol-based hand sanitizers containing methanol immediately and seek immediate medical attention if they experience any concerning symptoms by consumers. • Supervision on children using hand sanitizers, and keeping these products out of reach of children when not in use. • Not ingesting alcohol-based hand sanitizer products. • Evaluation for methanol poisoning in patients with compatible signs and symptoms or after having swallowed hand sanitize. • Coordination of health departments in all states with poison centers to identify cases of methanol poisoning. 	

Table 3
The origin of obtained articles

Country	Number of studies (out of 15)	References
Iran	12/15	[5,10,19,21,22,30,32–39]
USA	2/15	[10,38]
Australia	1/15	[31]

78 years [22]. Only a study in Australia reported one patient with methanol poisoning due to ingestion of the contents of methylated with containing of more than 60% methanol [31]. Two studies were from USA, that 9 patients with methanol poisoning in New Mexico in one of them [10], and 15 patients in another one [38]. It is worthy to mention that the reported patients and mortality are based on recognized and reported cases, and they certainly are not an accurate denominator due to many patients not receiving medical care or not being recognized by providers.

The recent outbreak is the largest methanol mass poisoning outbreak throughout Iran and the world in recent decades. Methanol mass poisoning outbreak has previously been reported in Iran (eg, in Shiraz, in 2004 with 62 poisoned and 11 dead, and Rafsanjan in 2013 with 694 cases of poisoning and 6 dead). Methanol mass poisoning outbreaks have also been reported by other countries including Sudan (in 2011 with 137 poisoned and 71 dead), Czech Republic (in 2012 with 121 poisoned cases and 20 dead), and Pakistan, Turkey, Libya, Indonesia, and Kenya [37].

4.2. Clinical findings and patients' management

In the reviewed studies, the reported poisoned patients and deaths were based on patients' histories, clinical symptoms, blood tests, toxicology tests, and autopsies. Morbidity and mortality in methanol poisoning are most prevalent amongst young and healthy people [30]. Most of studies mentioned the clinical and paraclinical findings in patients with methanol poisoning. Visual impairment especially blindness, severe anion-gap metabolic acidosis, gastrointestinal symptoms (such as; abdominal pain, nausea, and vomiting), and death were the most suggestive findings in these patients [19,21,31–33,38].

It was documented that visual impairment, metabolic acidosis with an elevated anion gap, and acute kidney injury are reported very specific presentations of methanol poisoning. However, difficulty breathing,

Table 5
Suggestive treatments in patients with methanol poisoning

Suggestive treatments
<ul style="list-style-type: none"> • Supportive and palliative care • Correction of acidosis • Administration of an alcohol dehydrogenase inhibitor (e.g., fomepizole: a competitive inhibitor of alcohol dehydrogenase) • Ethanol • Frequent hemodialysis • Poison Center consultation

pupillary dilation, hypotension, agitation, confusion, headache, difficulty walking, stomachache, diarrhea, jaundice, nausea and sometimes blood vomiting, leg cramps, and weakness was not specific for methanol poisoning [41]. Triad of visual impairment, gastrointestinal symptoms and metabolic acidosis in 6–24 h were mentioned in Sefidbakht et al.'s study [21]. Yip et al. said that vision loss results from the direct toxic effect of anion metabolite of methanol, known as formate, on the optic nerve [38]. Central nervous system involvement such as unconsciousness, headache and seizure were also reported [21,31,33,38].

Severe anion-gap metabolic acidosis is the common laboratory finding and diagnostic in methanol poisoned patients [10,21,31,35,38]. Welle et al. reported that an anion gap metabolic acidosis is commonly seen in large ingestions, but like serum osmolar gap, does not rule out toxic alcohol poisoning. Since methanol is less lipophilic than ethanol, toxicity can present without the typical intoxicating features of ethanol [10]. It was declared by Yip et al. that clinical presentations of methanol and ethanol poisoning are similar (e.g., headache, blurred vision, nausea, vomiting, abdominal pain, loss of coordination, and decreased level of consciousness), but patients with methanol poisoning could develop severe anion-gap metabolic acidosis, seizures, and blindness [38].

Nikoo et al. assessed electrocardiogram (ECG) findings in these patients that the most common of them were J point elevation, U wave, QTc prolongation, fragmented QRS, Brugada pattern, ST elevation myocardial infarction, Osborn wave, atrioventricular block, and sinus tachycardia [35]. In another study, the authors stated that Brugada Phenocopy is a novel marker of mortality in patients with methanol poisoning [39].

Iranpour et al. and Sefidbakht et al. mentioned the radiological finding in these patients [21,33]. Hemorrhagic and non-hemorrhagic necrosis of basal ganglia, white matter necrosis and diffuse brain edema may

Table 4
Clinical and paraclinical findings in patients with methanol poisoning

Clinical findings	Laboratory findings	ECG findings	Imaging Findings
<ul style="list-style-type: none"> • Triad of visual impairment, gastrointestinal symptoms and metabolic acidosis in 6–24 h. • Permanent disability • Central nervous system involvement: <ul style="list-style-type: none"> • Unconsciousness • Altered mental status • Decreased responsiveness • Unresponsive seizure • Headache • Vertigo • Visual disturbance: <ul style="list-style-type: none"> • Blurred vision • Near-total vision loss • Blindness • Gastrointestinal tract involvement: <ul style="list-style-type: none"> • Abdominal pain • Nausea • Vomiting • Dyspnea • End organ failure • Death 	<ul style="list-style-type: none"> • Severe anion-gap metabolic acidosis 	<ul style="list-style-type: none"> • The most common ECG findings: <ul style="list-style-type: none"> • J point elevation • U wave • QTc prolongation • Fragmented QRS • Brugada pattern • ST elevation myocardial infarction • Osborn wave • Atrioventricular block • Sinus tachycardia 	<ul style="list-style-type: none"> • An axial nonenhanced brain computed tomography (CT) scan: <ul style="list-style-type: none"> • Hemorrhagic and non-hemorrhagic necrosis of basal ganglia • White matter necrosis • Diffuse brain edema • Bilateral symmetrical decreased density of lentiform nuclei, especially putamina • Massive hemorrhage in the left lentiform nucleus • Axial T2 weighted MR images of the brain: <ul style="list-style-type: none"> • Increased signal intensity on T2-weighted sequence • Diffusion weighted imaging • Symmetrical increased signal intensity of basal ganglia • Putaminal involvement • Resorption of infarcted putamen in later stages

Table 6

The causes of methanol poisoning during COVID-19 pandemic (3P)

Public	Physicians	Policy makers
<ul style="list-style-type: none"> Lack of public awareness about the prevention and treatment of COVID-19. Lack of public awareness about the different types and uses of alcohol. Society unawareness about the hazards of toxic alcohol. Not trust the organizations or agencies publishing the true information. Tend to rumors, myths and conflicting information, and harmful practices from unofficial communication channels and social media. Public misconception about ingestion, drinking or gargling alcohol-based in the hope of disinfecting the virus in the mouth or within their bodies and its protection against COVID-19. Alcoholic beverage through unlawful means such as personal home production and illegal imports from some neighboring countries. Making consumed alcoholic drinks at home or unauthorized workrooms and repackaged in famous brands containers. Shifting the use of methanol instead of ethanol by individuals who were previously using ethanol for the manufacturing of alcoholic beverages due to unprecedented shortage in ethanol because of the large industrial use of ethanol for the manufacturing of hand sanitizers. Fear from recognition or reporting to poison centers or state health departments in poisoned patients and arresting them. Decreasing sports activity due to closure of gyms and the mass advertisement to the public to remain home, which led to increase the use of alcohol drinks. 	<ul style="list-style-type: none"> Challenge in the taking an exposure history in patients with altered mental status. Unable to test for a blood methanol level in some hospitals. 	<ul style="list-style-type: none"> Faulty understanding and mismanagement by the ruling authorities. Reduction in the amount of ethanol on the market. The large industrial using ethanol for the manufacturing of hand sanitizers during the COVID-19 pandemic, following the shortage of it, shift people to use methanol instead of ethanol for the manufacturing of alcoholic beverages. Legal prohibiting of the production, distribution, and drinking of alcoholic beverage in some countries. Smuggled and illegally banding of selling, consuming, producing, and distributing alcoholic beverages in some counties. Increased accessibility and consumption of mainly methanol--containing homemade and bootleg types of alcohol. Discoloring the industrial alcohol by 5% sodium hypochlorite solution (Vitex®) and sale it instead of ethanol or drinking alcohol by profiteers. Access smuggled or illegally homemade alcoholic beverages that may use methanol instead of ethanol. Using methanol instead of ethanol because of its lower price and availability Sanctions on access to essential medicines and equipment. The shortage of medical care and diagnostic capacity to prevent COVID-19. Not having proper laboratory equipment to determine the blood concentration of toxic alcohols. Importance of early identification and initiation of treatment, which can be supplemented by "active case finding" by treating physicians and public health agencies.

Table 7

The summary of recommendations regarding prevention or reduction of methanol poisoning during COVID-19 pandemic (3P)

Public	Physicians	Policy makers
<ul style="list-style-type: none"> Buying only standardized products containing alcohol (ethanol) for disinfection from reliable sources. Not use methylated spirits in alcohol-based hand rubs. Stop using alcohol-based hand sanitizers containing methanol immediately and seek immediate medical attention if they experience any concerning symptoms by consumers. Supervision on children using hand sanitizers, and keeping these products out of reach of children when not in use. Using all alcohol-based hand sanitizers only for disinfecting hands and should never be ingested or swallowed. Continuing to monitor Food and Drugs Administration's guidance. Avoiding producing their own alcohol-based hand rubs. 	<ul style="list-style-type: none"> Familiarity of the clinicians especially those working in emergency departments with clinical and radiological presentations of methanol poisoning. Having high index of suspicion for methanol poisoning by physicians when evaluating adult or pediatric patients with reported swallowing of an alcohol-based hand sanitizer product or with symptoms, signs, and laboratory findings compatible with methanol poisoning. Obtaining medical management advice by physicians from their regional poison center. 	<ul style="list-style-type: none"> Developing appropriate scientific policies for the prevention of alcohol poisoning. Making proper arrangement and policies for alcohol consumption and trade. Raising public awareness about the fatal outcomes of consumption of counterfeit alcoholic beverages sold in the black market through broadcasting various educational programs. Educating people about different types of alcohol and the related health impacts, even if consuming alcohol is prohibited. Informing people that the available "ethanol" might actually be methanol. Warning about specific hand sanitizers that contain methanol. Alert people by internationally recognized references and guidelines to not to use methanol for disinfecting hands, skin, medical supplies, and surfaces (such as door handles, desks, floors, etc.). Warning and controlling to add color to methanol by manufacturers, so people can easily differentiate between methanol and ethanol (colorless). Making strengthen supervision over pharmaceutical companies for production of alcohol containing products by the Food and Drug Administration of Iran. Controlling the quality of alcoholic beverages by Food and Drug Administration. Monitoring rumors via mainstream media, hotlines, social media, SMS messages, focus groups, feedback from community influencers and community volunteers. Adhering to the WHO guidance on formulations of alcohol-based hand rubs.

Table 7 (continued)

Public	Physicians	Policy makers
		<ul style="list-style-type: none">• Informed people that there is no policy in the hospitals in Iran to report alcohol users to the justice authorities and that this information is considered highly confidential.• Making amendments to the law for production, sale, and consumption of alcohols in order to improve the society health and prevent the production of toxic alcohols as beverages by legislators in Iran.• Publishing updates of affected population by emergency management officials about risk management and health and safety issues to mitigate uncertainty and rumors.• Encouraging the public by emergency management officials to remain skeptical about information coming from unofficial channels.• Including social media strategy in effective communication plan.• Improvement the surveillance and early warning systems for alcohol poisoning.• Cooperation between authorities at the local, national, and international levels to combat the illicit alcohol.• Providing essential facilities for timely diagnosis and treatment of poisonings.• Providing proper training of poisoning course in medical education.• Prosecuting ruling authorities for the methanol outbreaks.• Increasing unstructured leisure time.

lead to a serious prognosis [21]. Moreover, it was mentioned that bilateral necrosis of basal ganglia is one of the most common radiological finding. Putaminal involvement due to decreased blood flow through the basal vein of Rosenthal as the result of hypotension or accumulation of high concentrations of formic acid is expected. The resorption of infarcted putamen results in cystic cavities at the site of injury in later stages. These changes can be revealed in the brain computed tomography (CT) scan, but magnetic resonance imaging (MRI) can illustrate these in the best way [33]. Taheri et al. reported that 66.6% of patients with acute methanol poisoning had abnormal findings in brain CT scan [42]. They indicated that in addition to clinical and laboratory findings, the presence of putamen hemorrhage and subcortex white matter necrosis, which are detectable in brain CT scans of patients with acute methanol poisoning, are associated with poor outcomes. Therefore, this modality will be useful for physicians [14]. Sefidbakht et al. also

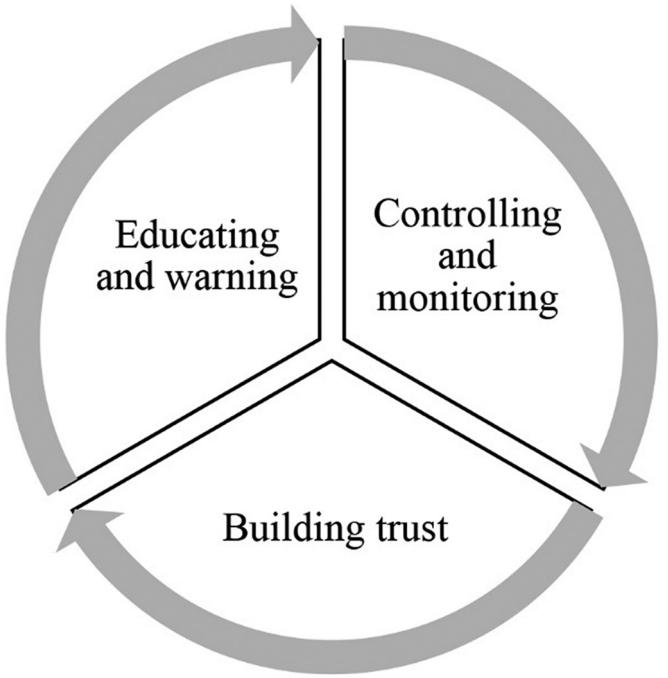


Fig. 2. Mapping the recommendations for policy makers to prevent or reduce the methanol poisoning outbreaks.

stated that CT scans and MRI reveal changes in patients with methanol poisoning, which can be helpful for physicians [18].

Supportive care and correction of acidosis should be started for all patients [36,38]. Fomepizole as a competitive inhibitor of alcohol dehydrogenase, in tandem with Poison Center consultation is mandatory for these patients. On the other hand, ethanol is second-line for treatment when fomepizole is unavailable [10]. Also, hemodialysis can improve hospital outcomes with toxin elimination [33,38,43].

Despite ethanol, untreated methanol poisoning can be fatal [38]. Four independent factors correlated with methanol toxicity severity were reported as severe acidosis ($\text{pH} < 7$) with $\text{QTc} > 500$, atrioventricular block, sinus tachycardia, and ST elevation myocardial infarction by Nikoo et al. [35]. Paasma et al. stated that $\text{pH} < 7$, coma ($\text{GCS} < 8$), and insufficient hyperventilation at the time of hospital admission are strong predictors of the final outcome [44]. Shadnia et al. found that coma, respiratory depression, PaCO_2 , and hyperglycemia were strong prognostic factors for undesirable survival in these patients [12]. Also, Hassanian-Moghaddam concluded that $\text{pH} < 7$ and coma at the time of admission, as well as delayed hospital admission (> 24 h), are associated with poor prognosis in these patients [45].

An issue that was mentioned is that many difficulties in the diagnosis and management of patients with alcohol poisoning because of lack of laboratory facilities to detect blood levels of toxic alcohols and their metabolites (ethanol, methanol, format, ethylene glycol, oxalate, and isopropanol concentrations), either gas chromatography with or without mass spectrometry confirmation (as gold standard method) or enzymatic assays; to measure plasma osmolality, chloride tests for calculating anion gap, and serum lactate level in most of teaching and referral hospitals in Iran, due to United States sanctions against this country. So, the toxicologists use blood gas analysis to detect these patients. In the management of methanol poisoning, administration of denatured ethanol with Bitrex (denatonium benzoate) orally or via a nasogastric tube as an antidote, folic acid as a cofactor, and hemodialysis for the elimination of toxic alcohols and its metabolites from the blood are recommended. It was reported that no intravenous ethanol, intravenous thiamine, Fomepizole (4-methylpyrazole), and Leucovorin

(Folinic acid) are available in Iran for the management of these patients, which can result of poor prognosis and death [41].

4.3. Causes

Multiple potential causes were raised by studies, which seems intertwined. Although there are wide ranges of disinfectant available, alcoholic disinfectants are the best disinfectants for viruses [46]. By starting the COVID-19 pandemic, sale of alcohol was increased 14–30% in several countries for disinfecting purposes [47]. Also, lack of public awareness about the prevention and treatment of COVID-19, different types of alcohol, hazards of toxic alcohol, and how to use it properly as well as fear and concern from being infected by the virus led to wide use of alcohol-based detergents, especially methanol [22,32,36–38]. Methanol has few disinfectant properties, and oral methanol consumption is associated with severe intoxication, blindness, and death [17]. Many people thought drinking or gargling alcohol-based drinks may protect and disinfect their bodies against COVID-19, when some evidence suggested that people infected with COVID-19 have the virus on their stool and gastrointestinal system [5,8,22,30,32,41,47]. It is worth mentioning that transcutaneous methanol poisoning is rare, that its absorption depends on many factors such as its form, contact time, dose, concentration, as well as size of the exposure area [38]. Although methanol poisoning outbreaks are historically described, relations to consumption of hand sanitizer have been rarely observed in the previous reports. Some of responsible organizations notified the public about the dangers of formulations of hand sanitizers marketed by some manufacturers, which used methanol and it was not listed as an ingredient [31,48].

Also, in this pandemic, people tend to rely upon rumors, myths and conflicting information, as well as harmful practices from unofficial communication channels and social media [21,22,30,32,34,37], because they do not trust the organizations or agencies publishing the true information, and they will not follow their advice [22,30,34]. Moreover, making consumed alcoholic drinks at home or unauthorized workrooms and repackaged in famous brands containers, and reduction in the amount of ethanol on the market because of the large industrial use of ethanol for the manufacturing of hand sanitizers led to shift the use of methanol instead of ethanol by individuals, who were previously using ethanol for the manufacturing of alcohol beverages [5,22,30,32,36,37]. Furthermore, it is worth mentioning that increased unstructured leisure time, decreasing sports activity due to closure of gyms, and the mass advertisement to the public to remain home have all led to increased use of alcohol drinks [5]. In addition, poisoned patients fear from recognition or reporting to poison centers or state health departments and arresting them. Hence, they may be reported to a poison center late, and they may refuse to provide an accurate medical history [38].

On the other hand, several studies reported the reasons at the policy makers' level. It seems that faulty understanding and mismanagement by the ruling authorities is one of the main cause of mass methanol poisoning [32]. Almost all existence strategies have mainly focused on palliative care and treating alcohol poisoning secondary to the consumption of illegal methanol at individual levels, not prevention programs [36]. Some studies mentioned that obtaining alcoholic drinks in some counties is far more difficult than in other countries in which selling, consuming, producing, and distributing of alcoholic beverages is illegal [5,30]. Consequently, people only access smuggled or illegally homemade alcoholic beverages. Ethanol is commonly used of for the manufacturing of alcohol beverages. During the COVID-19 pandemic, the large industrial use of ethanol for the manufacturing of hand sanitizers, following the shortage of it, these people shift to use methanol instead, since it is cheaper and widely available in the markets [5,36]. Some sellers of alcoholic beverages and disinfectants add bleach to methanol to discolor it, and sell it at a higher price instead of ethanol

[22,34,37]. Authorities are not taking the needed measures to address this issue, which led to the absence of public awareness.

Importance of early identification and initiation of treatment, which is better to be complemented by “active case finding” was recommended by studies [19]. But, sanctions on access to essential medicines and equipment, the shortage of medical care and diagnostic capacity, as well as not having proper laboratory equipment to determine the blood concentration of toxic alcohols were the main barriers [19,32,36]. Also, few studies mentioned that challenge in the taking an exposure history in patients with altered mental status and unable to test for a blood methanol level in some hospitals, which were raised at the physicians' level [19].

4.4. Recommendations

Studies recommended many solutions to decrease or prevent methanol poisoning during this pandemic, that we summarized them in 3P: People, Physicians, and Policy makers; however, they are intertwined.

At the people's level, people should only buy standardized products containing alcohol (ethanol) for disinfection and only from reliable sources [22], and they should not use methylated based in alcohol-based hand rubs [31]. They should stop using alcohol-based hand sanitizers containing methanol, immediately, and seek immediate medical attention if they experience any concerning symptoms [5,22,31,38]. Another recommendation is that they should not never gargle, swallow or ingest these detergents [22,30,34,37,38]. Also, they should avoid producing their own alcohol-based hand rubs as well as homemade alcoholic beverages [22,31,36]. Supervision on children using hand sanitizers, and keeping these products out of reach of children when not in use was another recommendation [21,38].

At the physicians' level, familiarity with clinical and radiological presentations of methanol poisoning by the clinicians, especially those working in emergency departments, was suggested. Physicians should have high index of suspicion for methanol poisoning when evaluating adult or pediatric patients with reported swallowing or gargling of an alcohol-based hand sanitizer product or with symptoms, signs, and laboratory findings compatible with methanol poisoning [10,33,38].

The most important recommendations in previous studies were focused on policy makers [19,22,30,31,36]. Developing appropriate scientific policies for the prevention of alcohol poisoning is the core [30]. We mapped the recommendations for policy makers in a figure which includes three categories; a) building trust; b) educating and warning; and c) controlling and monitoring.

It was stated by Aghababaeian that effective risk communication can help to avoid rumor and prevent personal and public health risks [22]. As was mentioned above, in this pandemic, people may rely upon rumors and misleading information, and harmful practices from unofficial communication channels and social media which encouraged them to drink or gargle alcohol to prevent or cure COVID-19 [22,30,32,34,37]. On the other hand, they did not trust the organizations or agencies publishing the true information. In this regard, building trust by policy makers is recommended [22]. In the second step, in the situations of crisis, to raise public awareness, timely and accurate news and information about the fatal outcomes of consumption of fake alcohols, as well as using reliable disinfectants must be provided to the people, and the consequences of the false information must be taken into account [8,36,37]. Also, they should know about different types of alcohol and should be informed that the available ethanol might actually be methanol, so they should be sensitizers from reliable markets [9,22,37]. In this regard, social media should widely use to educate the public about risk, risk management, and health and safety issues [21,22]. It is worth mentioning that informing people that there is no policy in the hospitals to report alcohol users to the justice authorities and this information is considered highly confidential, is highly recommended [22].

In regards of controlling and monitoring, it is necessary to develop regulatory and monitoring mechanisms during the process of manufacturing of sanitizers to verify the purity of alcohol-based hand sanitizers [22,32,46]. As was mentioned previously, methanol should not be used in hand sanitizers, because it is a highly toxic detergent, which can cause severe reactions when exposed to the skin, lungs or mouth [46]. Methanol staining by manufacturers should be mandatory so that people can easily distinguish between it and ethanol, which is colorless [22,32]. Another recommendation was the improving the surveillance and early warning systems for alcohol poisoning in the purpose of better controlling and monitoring [23]. Also, cooperation between authorities at the local, national, and international levels to combat the illicit alcohol should be more strengthen [22]. Moreover, providing diagnostic and therapeutic facilities at least for referral hospitals by policy makers is essential [41].

The policy makers should adhere to the WHO guidance on formulations of alcohol-based hand sanitizers, undertake a regular inspection of manufacturers and quality testing of sample hand sanitizers from the market, strength the supervision over pharmaceutical companies for production of alcohol containing products, as well as the sale of alcohol on the black markets [5,9,30,37].

4.5. Limitations

The main limitation of this systematic scoping review stems from the lack of high-quality evidence and interventional studies, and the provided causes and recommendations were based on the authors' experiences and opinions. None of the studies followed up the participants.

5. Conclusion

The results showed that the recent outbreak is the largest methanol mass poisoning outbreak throughout Iran and the world in recent decades. It seems that the causes of methanol poisoning during the COVID-19 pandemic are intertwined, and most of them are modifiable by health policy makers. Building trust, educating and warning, as well as controlling and monitoring are main three recommendation for prevention or reduction of methanol poisoning, which were mapped according to the previous evidences, and can guide administrators to design a comprehensive approach.

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Ethical issues

This study was approved by the vice-chancellor of research and technology (Grant No. 22000), as well as the local Ethics Committee (IR.sums.med.rec.1399.517) of Shiraz University of Medical Sciences.

Availability of data and material

Data sharing is not applicable to this article.

Standard protocol approvals, registrations, and patient consents

The Shiraz University of Medical Sciences Institutional Review Board approved this systematic review (IR.sums.med.rec.1399.517).

Systematic review registration number

The review protocol was not previously registered.

Declaration of Competing Interest

The authors declare that they do not have any conflict of interest.

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